1/17

PCT/IB2003/003487

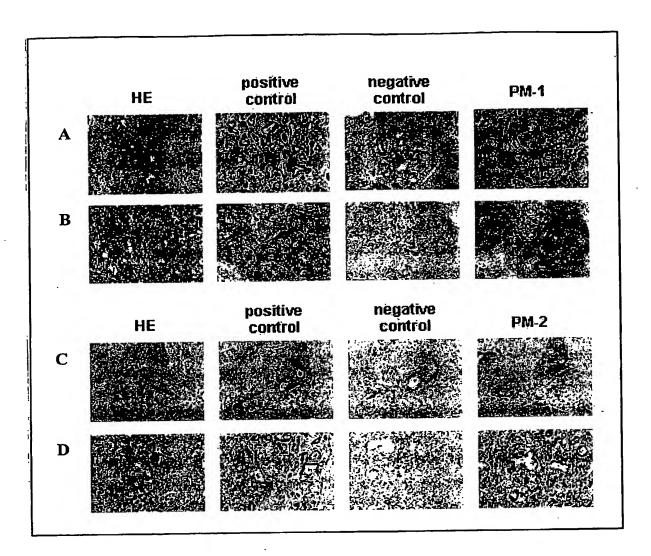
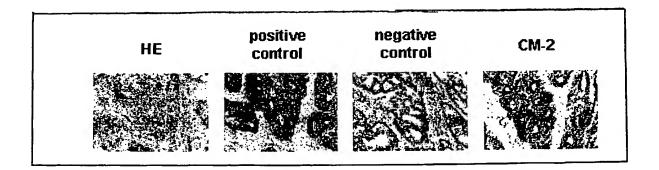


FIG. 1

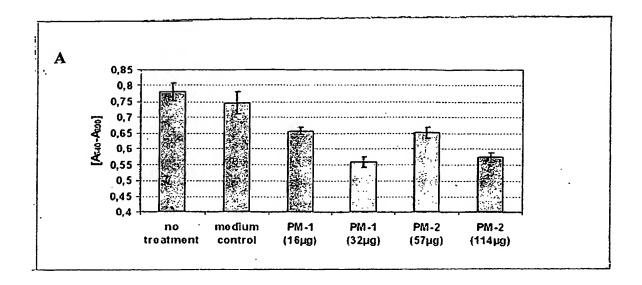
2/17

PCT/IB2003/003487



3/17





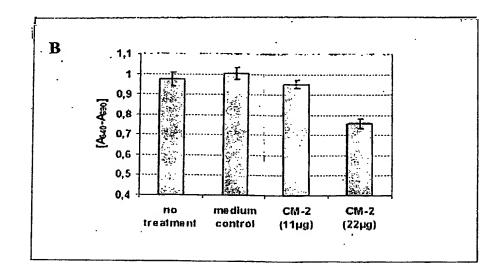
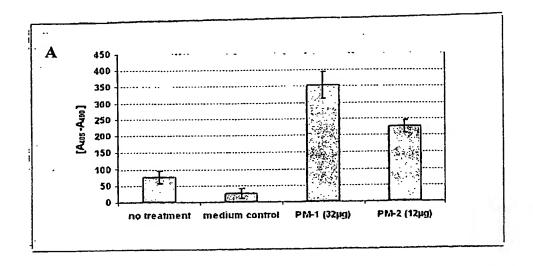


FIG. 3

4/17

PCT/IB2003/003487



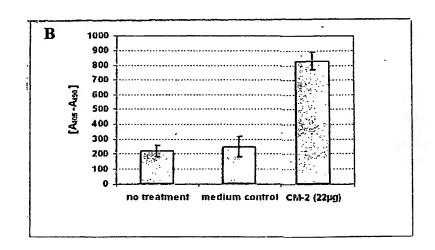


FIG. 4

5/17

PCT/IB2003/003487

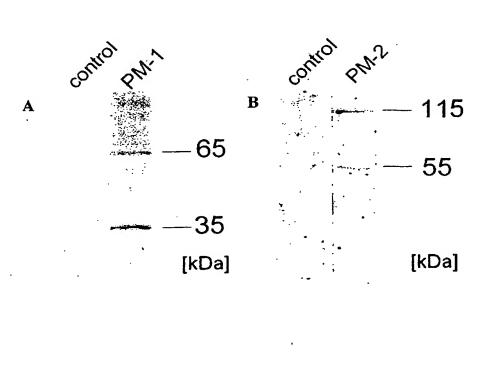
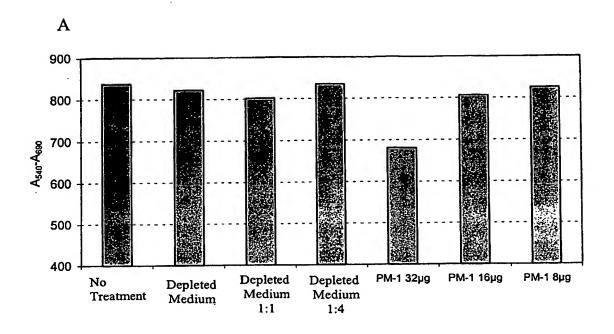


FIG. 5



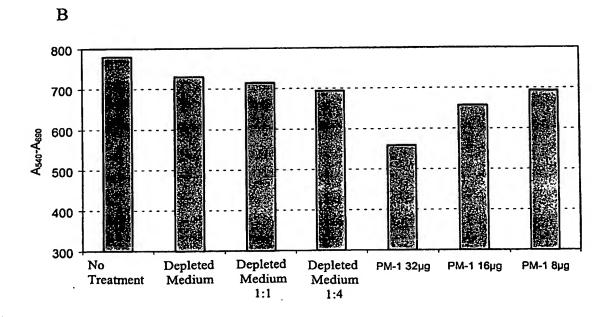


FIG. 6

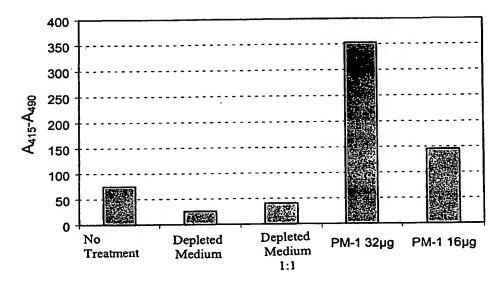
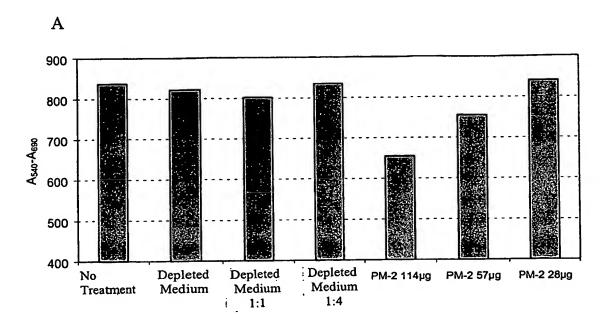


FIG. 7

PCT/IB2003/003487

8/17



, **B**

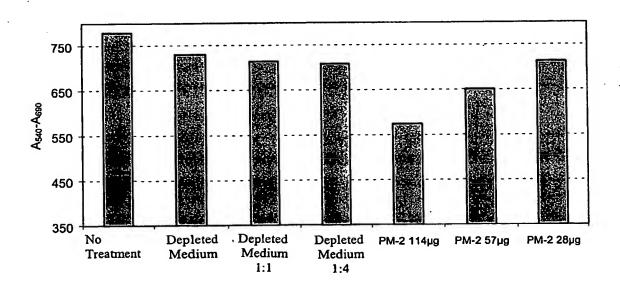


FIG. 8

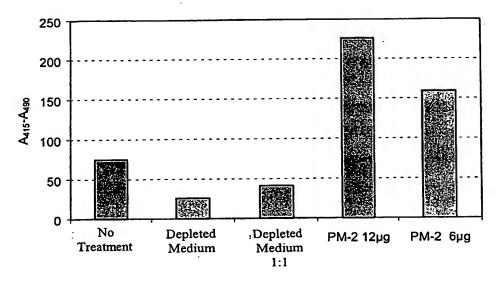
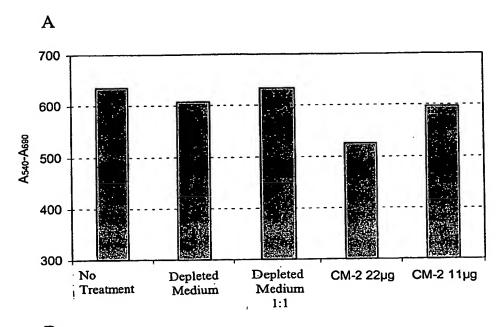


FIG. 9





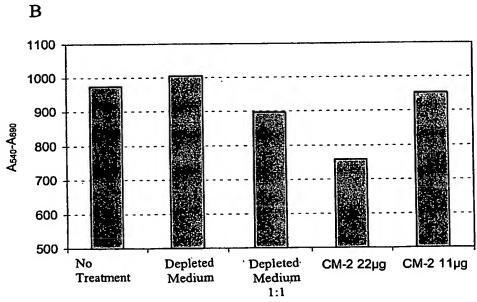


FIG. 10

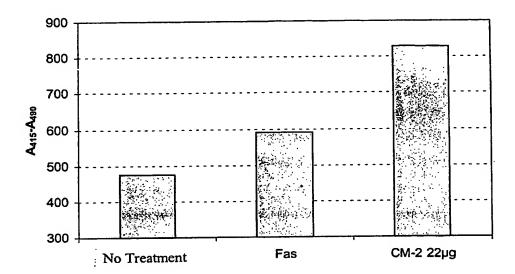


FIG. 11

12/17

PCT/IB2003/003487

PM-1 Light chain variable region sequence

tcc Ser 1	tat Tyr	gtg V al	ctg Leu	act Thr 5	cag Gln	cca Pro	ccc Pro	tcg Ser	gtg Val 10	tca Ser	gtg Val	tcc Ser	cca Pro	gga Gly 15	caa Gln	acg Thr	gcc Ala	agg Arg	atc Ile 20	60)
							CD											*==	222	120	,
acc Thr	tgc Cys	tct Ser	gga Gly	gat Asp 25	gca Ala	ttg Leu	cca Pro	aaa Lys	aaa Lys 30	tat Tyr	Pro	Tyr	tgg Trp	Tyr 35	Gln	Gln	aag Lys	Ser	Gly 40	120	,
									DR2												
cag Gln	gcc Ala	cct Pro	gtg Val	ctg Leu 45	gtc Val	atc Ile	tat Tyr	gag Glu	gac Asp 50	agc Ser	aaa Lys	cga Arg	ccc Pro	ser 55	G1A 888	atc Ile	cct Pro	gag Glu	aga Arg 60	180)
ttc Phe	tct Ser	ggc Gly	tcc Ser	agc Ser 65	tca Ser	Gl y 999	aca Thr	atg Met	gcc Ala 70	acc Thr	ttg Leu	act Thr	atc Ile	agt Ser 75	Gly 999	gcc Ala	cag Gln	gtg Val	gag Glu 80	240	D
										CD					_						
gat Asp	gaa Glu	gct Ala	gac Asp	tac Tyr 85	tac Tyr	tgt Cys	tac Tyr	tca Ser	aca Thr 90	Asp	agc Ser	agt Ser	ggt Gly	aat Asn 95	atg Met	tct Ser	tcg Ser	gaa Glu	ctg Leu 100	30	D
	cca Pro				Ser															31	8

10/520224 PCT/IB2003/003487

WO 2004/005351

13/17

PM-1 Heavy chain variable region sequence

	CDR1																			
999 Gly 1	tcc Ser	ctg Leu	aga Arg	ctc Leu 5	tcc Ser	tgt Cys	gca Ala	gcc Ala	tct Ser 10	gga Gly	ttc Phe	acc Thr	ttt Phe	agc Ser 15	agc Ser	tat Tyr	gcc Ala	atg Met	agc Ser 20	60
		CDR2																		
tgg Trp	gtc Val	cgc Arg	cag Gln	gct Ala 25	cca Pro	999 Gly	aag Lys	G1 y .999	ctg Leu 30	gag Glu	tgg Trp	gtc Val	tca Ser	gct Ala 35	att Ile	agt Ser	ggt Gly	agt Ser	ggt Gly 40	120
ggt Gly	agc Ser	aca Thr	tac Tyr	tac Tyr 45	gca Ala	gac Asp	tcc Ser	gtg Val	aag Lys 50	ggc Gly	cgg Arg	ttc Phe	acc Thr	atc Ile 55	tcc Ser	aga Arg	gac Asp	aat Asn	tcc Ser 60	180
aag Lys	aac Asn	acg Thr	ctg Leu	tat Tyr 65	ctg Leu	caa Gln	atg Met	aac Asn	agc Ser 70	ctg Leu	aga Arg	gcc Ala	gag Glu	gac Asp 75	acg Thr	gcc Ala	gta Val	tat Tyr	tac Tyr 80	240
				CDR	.3															
tgt Cys	gcg Ala	aaa Lys	gat Asp	tca Ser 85	ttt Phe	cgt Arg	gaa Glu	gga Gly	ccc Pro 90	tgg Trp	ggc Gly	cag Gln	gga Gly	acc Thr 95	ctg Leu	gtc Val	acc Thr			294

PCT/IB2003/003487

14/17

PM-2 Light chain variable region sequence

cag Gln 1	tct Ser	gcc Ala	ctg Leu	act Thr 5	cag Gln	cct Pro	gct Ala	tcc Ser	ctc Leu 10	tct Ser	gca Ala	tct Ser	cct Pro	gga Gly 15	gca Ala	tca Ser	gcc Ala	agt Ser	Leu 20	60
acc Thr	tgc Cys	acc Thr	ttg Leu	cgc Arg 25	agt Ser	ggc Gly	atc Ile	aat	gtt Val	gat	acc Thr	tac Tyr	agg Arg	ata Ile 35	tac Tyr	tgg Trp	tac Tyr	cag Gln	cag Gln 40	120
aag Lys	cca Pro	999 Gly	agt Ser	cct Pro 45	ccc Pro	cag Gln	tat Tyr	ctc Leu	ctg Leu 50	agg Arg	tac Tyr	aaa Lys	tca	gac Asp 55	tca	gat Asp	aag Lys	cag Gln	aag Lys 60	180
ggc Gly	tct Ser	gga Gly	gtc Val	ccc Pro 65	agc Ser	cgc Arg	ttc Phe	tct Ser	gga Gly 70	tcc Ser	aaa Lys	gat Asp	gct Ala	tcg Ser 75	gcc Ala	aat Asn	gca Ala	GLY	att Ile 80	240
tta Leu	ctc Leu	atc Ile	tct Ser	999 Gly 85	ctc Leu	cag Gln	tct Ser	gag Glu	gat Asp 90	gag Glu	gct Ala	gac Asp	tat Tyr	tac Tyr 95	Cys	atg Met	att Ile	tgg	cac His 100	300
agc Ser	agc Ser	gct Ala	tgg Trp	gtg Val 105	ttc Phe	ggc Gly	gga Gly	G1y 999	acc Thr 110	Lys	ctg Leu	acc Thr	gtc Val	cta Leu 11	Gra					348

15/17

PCT/IB2003/003487

PM-2 Heavy chain variable region sequence

														OR1		_				
999 Gly	tcc Ser	ctg Leu	aga Arg	Leu	tcc Ser	tgt Cys	gca Ala	gcc Ala	ser	gga Gly	ttc Phe	acc Thr	ttt Phe	agc Ser 15	agc Ser	tat Tyr	gcc Ala	atg Met	agc Ser 20	60
1				5					10								CDR			
tgg Trp	gtc val	cgc Arg	cag Gln	gct Ala 25	cca Pro	GJÀ 333	aag Lys	G J À 333	ctg Leu 30	gag Glu	tgg Trp	gtc val	tca Ser	gct Ala 35	att Ile	agt Aer	ggt Gly	agt Ser	ggt Gly 40	120
ggt Gly	agt Ser	aca Thr	tac Tyr	tac Tyr 45	gca Ala	gac Asp	tcc Ser	gtg Val	aag Lys 50	ggc Gly	cgg Arg	ttc Phe	acc Thr	atc Ile 55	tcc Ser	aga Arg	gac Asp	aat Asn	tcc Ser 60	180
aag Lys	aac Asn	acg Thr	ctg Leu	tat Tyr 65	ctg Leu	caa Gln	atg Met	aac Asn	agc Ser 70	Leu	aga Arg	gcc Ala	gag Glu	gac Asp 75	acg Thr	gcc Ala	gta Val	tat Tyr	tac Tyr 80	240
									CI	DR3					_			_		
tgt Cys	gcg Ala	aaa Lys	ggt Gly	999 Gly 85	gcc Ala	gaa Glu	ggc Gly	tgg Trp	tac Tyr 90	GIU	tac Tyr	tac Tyr	tac Tyr	tac Tyr 95	ıyı	ggt Gly	atg Met	gac Asp	gtc Val 100	300
tgg Trp	ggc Gly	caa Gln	Gly 999	acc Thr 105	ctg	gtc Val														321

16/17

PCT/IB2003/003487

CM-2 Light chain variable region sequence

cag Gln 1	tct Ser	gcc Ala	ctg Leu	act Thr 5	cag Gln	cct Pro	gcc Ala	tcc Ser	gtg Val 10	tct Ser	GJA 333	tct Ser	Pro	gga Gly 15	Gln	Ser	Ile	Thr	Ile 20	80
									DRI					_						
tcc Ser	tgc Cys	act Thr	gga Gly	acc Thr 25	agc Ser	agt Ser	gac Asp	gtt Val	ggt Gly 30	ggt Gly	tat Tyr	aac Asn	tat Tyr	gtc Val 35	tcc Ser	tgg Trp	tac Tyr	caa Gln	cag Gln 40	120
											CD	R2		_						
cac His	cca Pro	ggc. Gly	aaa Lys	gcc Ala 45	ccc Pro	aaa Lys	ctc Leu	atg Met	att Ile 50	tat Tyr	gat Asp	gtc Val	agt Ser	aat Asn 55	cgg Arg	ccc Pro	tca Ser	GJA 333	gtt Val 60	180
tct Ser	aat Asn	cgc Arg	ttc Phe	tct Ser 65	ggc Gly	tcc Ser	aag Lys	tct Ser	ggc Gly 70	aac Asn	acg Thr	gcc Ala	tcc Ser	ctg Leu 75	acc Thr	atc Ile	tct Ser	gga Gly	ctc Leu 80	240
														CDR					-	
cag Gln	gct Ala	gag Glu	gac Asp	gag Glu 85	gct Ala	gat Asp	tac Tyr	tac Tyr	tgc Cys 90	agc Ser	tca Ser	aaa Lys	aga Arg	agc Ser 95	agc Ser	aac Asn	act Thr	cta Leu	gta Val 100	300
ttc Phe	ggc Gly	gga Gly	G1 y 999	acc Thr 105	aag Lys	ctg Leu	acc Thr	gtc Val	cta Leu 110											330

17/17

PCT/IB2003/003487

CM-2 Heavy chain variable region sequence

			•																	
aaa Lys 1	aag Lys	ccc Pro	Gly Ggg	gag Glu 5	tct Ser	ctg Leu	agg Arg	atc Ile	tcc Ser 10	tgt Cys	aag Lys	ggc Gly	tct Ser	gga Gly 15	tac Tyr	agt Ser	ttt Phe	acc Thr	acc Thr 20	60
tac Tyr	tgg Trp	atc Ile	ggc Gly	tgg Trp 25	gtg Val	cgc Arg	cag Gln	atg Met	ccc Pro 30	G1y 999	aaa Lys	ggc Gly	ctg Leu	gag Glu 35	tgg Trp	atg Met	G1y 999	atc Ile	atc Ile 40	120
		CD																		
tat Tyr	cct Pro	ggt Gly	gac Asp	tct Ser 45	gat Asp	acc Thr	aga Arg	tac Tyr	agc Ser 50	ccg Pro	tcc Ser	ttc Phe	caa Gln	ggc Gly 55	cag Gln	gtc Val	acc Thr	atc Ile	tca Ser 60	180
gcc Ala	gac Asp	acg Thr	tcc Ser	atc Ile 65	agt Ser	acc Thr	gcc Ala	tac Tyr	ctg Leu 70	cag Gln	tgg Trp	agc Ser	agc Ser	ctg Leu 75	aag Lys	gcc Ala	tcg Ser	gac Asp	acc Thr 80	240
												CDR	3							
gcc Ala	ata Ile	tat Tyr	tac Tyr	tgt Cys 85	gcg Ala	agg Arg	gag Glu	gtc Val	tat Tyr 90	act Thr	ggc	cga Arg	aac Asn	tac Tyr 95	tac Tyr	tac Tyr	tac Tyr	ggt Gly	ctg Leu 100	300
gac Asp	gtc Val	tgg Trp	ggc	caa Gln 105	gga Gly	acc Thr	ctg Leu	gtc Val												327